Visna in a UK flock and the biosecurity risk arising from the onward sale of likely infected pedigree stock

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CASE REPORT

Food/farmed animals

Visna in a UK flock and the biosecurity risk arising from the onward sale of likely infected pedigree stock

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Abstract

Small Ruminant Lentivirus infections in sheep most commonly present with respiratory signs (maedi) and indurative mastitis, while primary neurological signs (visna) have rarely been reported in Great Britain. Most reports of visna describe signs referable to myelitis, although central signs associated with encephalitis may feature. In this case, visna was diagnosed in a 4-year-old ewe in a small pedigree sheep flock, recently imported to GB from northern Europe. Initial clinical findings were of a head tilt, circling, facial tremors and a unilaterally reduced menace response. These neurological signs progressed to include hyperaesthesia, ipsilateral hemiparesis and recumbency. Flock level infection had recently been diagnosed by serology, and the diagnosis in this individual case was confirmed by serology and histopathology. The subsequent sale of animals from the flock through a large national auction and at private sales raises significant ethical questions and serves as a reminder of the importance of biosecurity precautions.

BACKGROUND

Maedi visna (MV) is a chronic, fatal disease of sheep caused by infection with small ruminant lentivirus (SRLV). Clinical signs most often progress slowly, and, anecdotally, flocks have often reached seroprevalences of at least 50% before the disease is identified. However, in the preceding period, subclinical disease is likely to have caused significant economic losses.[1] MV is therefore commonly considered an 'Iceberg disease', where clinical cases represent only a small fraction of the flock level impact. The accurate and timely identification of clinical cases is important, especially in flocks that do not routinely screen for such iceberg diseases. Maedi (lymphofollicular pneumonia resulting in dyspnoea) is the most common presentation of infection with SRLV in sheep; however, there have been three historic reports of visna (progressive inflammatory disease of the central nervous system) in GB.[2–4] The visna presentation was relatively common when MV was first seen in Iceland[5] and has been more recently reported in outbreaks in Spain.[6] It is hypothesised that geographical variation in the signs seen may represent a combination of variation in both susceptibility of sheep breeds and virus subtypes.[7,8]

Over the past 10 years, the number of Premium Sheep and Goat Health Scheme (PSGHS) member flocks in which SRLV infection has been identified has been less than 1%, and in that time the number of member flocks has risen from 2500 to 3261 (SRUC, personal communication). However, this is a small fraction of the total number of flocks (approximately 35,000),[9] and there have been concerns in the British veterinary and farming press following high-profile cases that have had devastating impacts in both commercial and pedigree flocks.[10–17] It is therefore extremely important that farmers and vets consider the risks of introducing MV into their flocks through the purchase of replacement animals.

This article describes the diagnosis of a case of visna in a flock of pedigree sheep recently imported into Great Britain, provides detailed mapping of the neuropathological lesions present in this case and discusses the biosecurity risks arising from the subsequent sale of animals from the flock at a large UK auction and through private sales. This serves as an important reminder of: the variable clinical presentation of MV; the biosecurity risks presented by bought in replacement animals; and the ethical challenges veterinary surgeons commonly face in practice.

The location of the farm, the name of the referring veterinary surgeon and the breed of sheep have been redacted to maintain the flock owner's anonymity.

CASE PRESENTATION

A flock of approximately 30 pedigree ewes was imported into GB in early 2018, following the relocation of their owner from northern Europe. The owner had intended to establish the

flock as MV accredited under the PSGHS in order to maximise the value of lambs sold as pedigree replacements or terminal sires. However, at the first qualifying test, an SRLV seroprevalence of approximately 50% had been identified. The owner had not noticed signs of clinical disease or reduced performance in the flock and decided not to immediately pursue options for elimination or reduction of MV within the flock.

In July 2018, the referring veterinary surgeon was called to examine a 4-year-old ewe displaying neurological signs. This ewe had been seronegative for SRLV on the first qualifying test (carried out 6 months previously). The ewe had been housed between arrival in the UK and lambing in April and was fed silage and compound concentrate feed during that period. She had lambed twins in April and was then turned out onto low ground pasture co-grazed with cattle, with some additional concentrate feeding provided. The lambs were not weaned at the time of the first clinical examination. There was no recognised problem with ticks on the holding.

LEARNING POINTS/TAKE-HOME MESSAGES

- The wide range of clinical signs and insidious nature of SRLV/maedi-visna may lead to underdiagnoses.
- Visna most commonly presents with myelitis resulting in a unilateral hind paresis; however, it may also present with more variable central neurological signs associated with encephalitis.
- The sale of lambs from this flock through a large auction mart and private sales serves as a reminder of the importance of biosecurity precautions.

INVESTIGATIONS

Differential diagnosis

On clinical examination the ewe exhibited a head tilt and circling to the right, mild tremors of the muzzle and ears bilaterally, and a reduced menace response on the left-hand side (limited response to threatening the eye, despite normal palpebral and pupillary light reflexes). The ewe was in moderate to lean body condition score (2/5), she was not pyrexic, and systemic clinical examination findings were unremarkable. These clinical signs suggested either focal encephalitis, or a right-sided space occupying lesion in the right cerebral hemisphere and brainstem. These signs could also be the result of otitis media, if it were not for the reduced menace response and facial tremors.

Listerial encephalitis was initially considered the most likely differential diagnosis, although there was no supportive history of recent silage feeding nor any trigeminal or facial nerve signs. Despite the high flock seroprevalence, visna was considered less likely due to this individual's previous negative serology (ID-Vet ELISA [Innovative Diagnostics], approximately 6 months prior), and the relative rarity of the encephalitic form of this disease in GB. Flavivirus encephalitis (louping ill) was considered unlikely due to the clinical presentation and lack of knowledge of ticks on the farm; however, the timing of presentation could have been consistent with novel exposure to the virus following the first emergence of ticks since moving to the farm in the winter. Central sarcocystosis was considered as another possible cause of encephalitis, given dogs had access to the fields and housing, although the clinical signs and the age of the ewe militated against this possibility.

Treatment

As the diagnosis was unclear from the clinical exam, the referring veterinary surgeon initiated non-specific empirical treatment with dexamethasone 0.1 mg/kg intravenous, once (Dexadreson; MSD); thiamine 10 mg/kg intravenous, once (Vitamin B1; Bimeda); andpenicillin/streptomycin 8/10 mg/kg intramuscular once daily for 7 days (Pen & Strep; Norbrook).

Outcome and follow-up

The ewe was re-examined at the end of the course of treatment, by which point the facial tremors had become more severe, and there was now left hind paresis and a more general ataxia (although ataxia can be difficult to assess alongside paresis). The progression of clinical signs to include signs referable to the spinal cord led to visna being considered a more likely diagnosis and a referral visit was arranged for 3 days later.

At the referral visit, the clinical signs were as described previously, with an additional left-sided facial paresis (dropped ear, muzzle deviation and absent palpebral reflex), bilateral facial hyperaesthesia and left-sided hemiparesis (including increased patellar reflex). The ewe was recumbent, but alert, and it was decided that euthanasia was required. Blood samples were taken at the point of euthanasia, and a post-mortem lumbosacral cerebrospinal fluid (CSF) tap was performed immediately after.

Nogross abnormalities were seen on inspection of the brain on post-mortem examination. The CSF was colourless, non-turbid and did not form a stable foam on shaking, suggesting protein levels were normal.[18] The CSF leukocyte concentration was 3.3/μl, which is within the normal range for ovine CSF (<10/μl).[18] Negative pressure within the thorax was present on incision of the diaphragm; however, the lungs were grossly enlarged with rib impressions and diffuse congestion. Multifocal < 1 mm diameter firm, grey nodules were present throughout the lung parenchyma on cut section, and small volumes of yellowish exudate were present in some airways. The mammary gland was grossly normal. No joint distension was noted, although there was a 1-cm semilunar area of thinning of articular cartilage on lateral aspect of the right humeral head.

Serology of the blood taken at the time of euthanasia was positive for antibody against MV using both the ID-Vet ELISA (Innovative Diagnostics) and the ElitestELISA (Hyphen Biomed).

Histology of the lungs (Figure 1) showed scattered areas of mostly perivascular infiltration by lymphocytes, occasionally

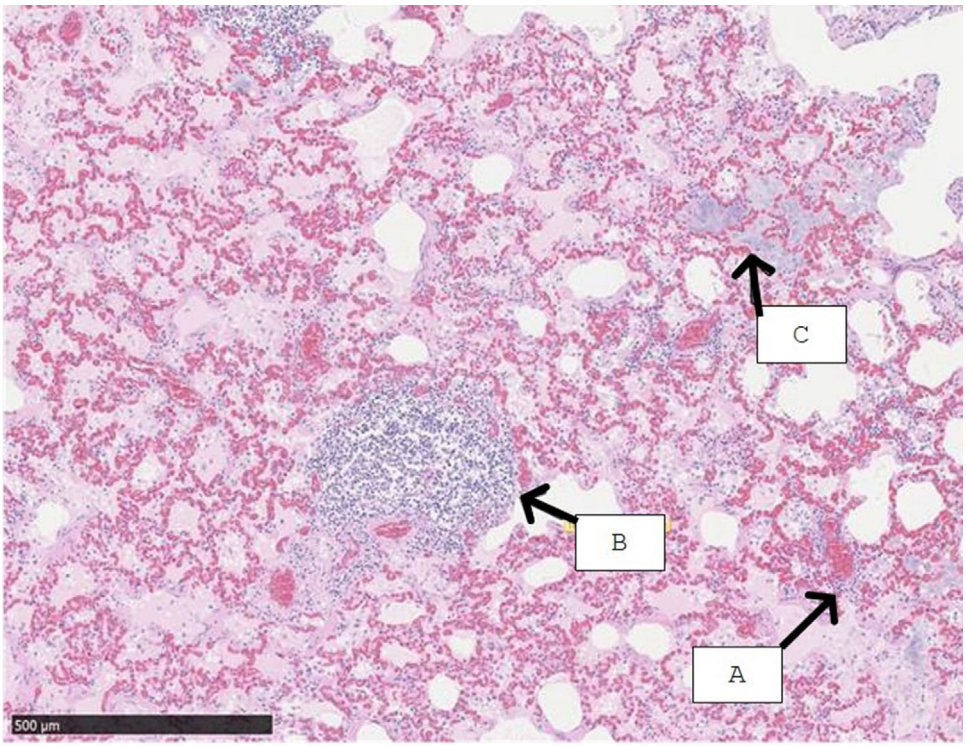

FIGURE 1 High power section of lung (H&E stain) showing: (a) lymphocytic infiltration; (b) a tertiary lymphoid follicle; and (c) bacterial colonies

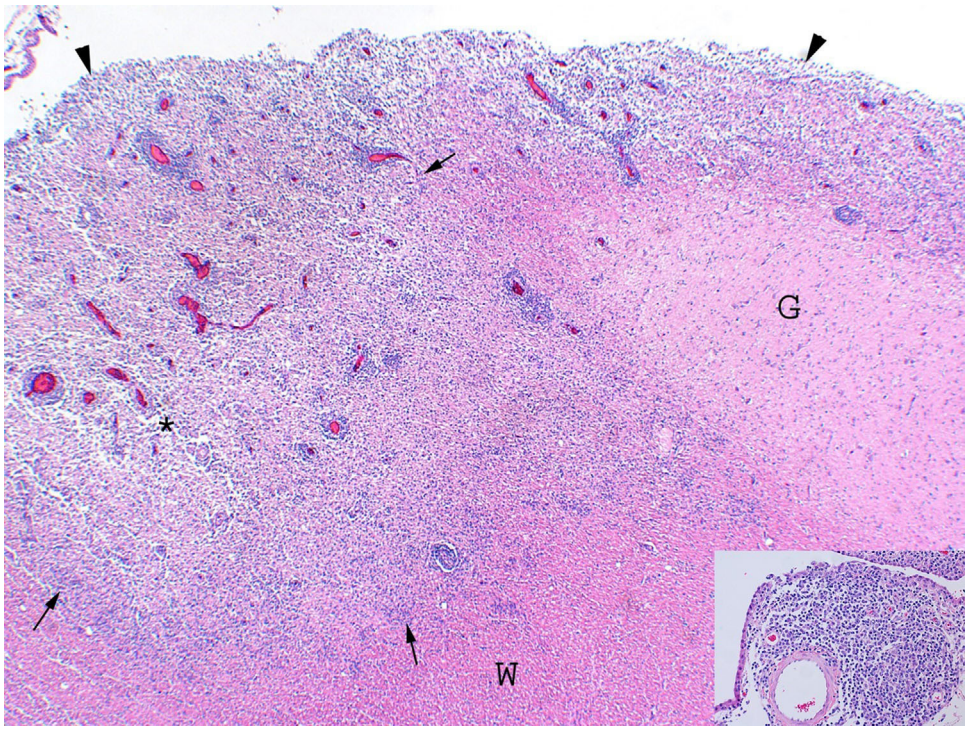

FIGURE 2 Brain, level of rostral lateral ventricle. Extensive leucoencephalitis with rarefaction and loss of neuroparenchymal structure, including myelin, and gliosis in white matter surrounding lateral ventricle (between arrows) with an area of incipient cavitation (asterisk), accompanied by ependymitis (arrowheads). There is sparing of deeper white matter (W) and of adjacent grey matter (G). Inset: Lymphofollicular choroid plexitis in adjacent lateral ventricle

forming tertiary lymphoid follicles. In addition, there were multifocal colonies of bacteria (cocci) in the pulmonary interstitium and inside alveolar lumens, associated with loss of structure of adjacent tissue. These histological findings are consistent with a diagnosis of maedi, with secondary bacterial pneumonia, liquefactive necrosis and possible agonal inhalation. It is interesting to note that the ewe had shown no clinical signs indicating respiratory disease, despite this significant pathology.

Histology of the brain (Figure 2) showed severe bilateral asymmetrical lymphocytic and necrotising leucoencephalitis. Perivascular lymphocytic infiltration involved the following areas: periventricular white matter (moderate to severe), fornix (severe), frontal cortex (focal, mild) and brainstem

(severe, multifocal extensive), accompanied by gliovascular activation, occasional neuronal chromatolysis and rare axonal swellings. In addition, in the periventricular cerebral white matter and cerebellar peduncles, more severe changes included extensive predominantly white matter rarefaction and incipient cavitation, oedema and infiltration by macrophages and multinucleated giant cells, extending to areas of ependymal attenuation and loss. Multifocal lymphofollicular choroid plexitis was also present. These histological findings are typical of visna encephalitis.

The combination of serological results and histopathology confirm the diagnosis of visna, alongside maedi and secondary bacterial pneumonia. In light of these findings, the owner planned to separate seropositive and seronegative animals, in the hope of eventually establishing a separate MV-accredited flock within the larger holding. However, this approach may prove challenging given the increased number of breakdowns in accredited flocks with non-accredited stock on the same holding, and the stricter accreditation rules for such flocks.[19,20] Eighteen months after the initial diagnosis, the flock management remains unchanged, and no further serological testing has been performed. In the intervening period, the owner noted at least two similar neurological cases (although these were not submitted for necropsy) and several cases of indurative mastitis.

Despite veterinary advice to the contrary, the owner has subsequently sold lambs as non-accredited pedigree stock at a large national auction and in private sales, including to neighbouring farms. The lambs were not tested by the owner, and their infection status was unknown at the point of sale, therefore the owner does not appear to have made any false claims about their health status. However, there is evidence of a heritable component to SRLV susceptibility, prenatal and lactogenic vertical infection and efficient horizontal transmission between lambs.[21–23] It is therefore possible that a significant proportion of these lambs were infected. To date, the owner has had only one lamb returned by the purchaser following a positive serology result during post-purchase quarantine.

DISCUSSION

Visna has been rarely diagnosed in the GB with only three reports found in the literature.[2–4] Where visna has been reported it has primarily presented with the spinal form (hind paresis), although the initial signs displayed in this case fit previous descriptions of the encephalitic form of the disease.[4,24] A survey of GB flocks in 2010 found flock level prevalence of MV to have doubled from 1.4% in 1995/6 to 2.8% (95% CI 1.6–3.9) in 2010; and it was estimated that there were approximately 110,000 infected breeding sheep in GB in 2010.[25] Minor annual increases in VIDA submissions were reported in 2016, but there may be significant under-reporting given the insidious nature of the disease.[23,25,26] A new national survey would help assess current within- and between-flock prevalence and guide advice regarding the potential impact of the disease.

Although MV and caprine arthritis and encephalitis were previously considered to be caused by two separate viruses, genetic analysis suggests they are both caused by a single SRLV, albeit with five types (A-E) that show varying degrees of host species tropism. These types are further divided into subtypes, with some geographical clustering. Alongside differences in management and host genetics, this may be partly responsible for geographical variation in tissue tropism and clinical signs of MV.[7,8] This raises questions about the strain of the virus present in this imported flock, although genotyping was not performed in this case.

It is interesting that this ewe was seronegative on the initial screen 6 months previously. This influenced the initial differential diagnosis; however, it is not surprising for new cases to develop over a 6-month period in a flock with a 50% seroprevalence. Given the timeframe, this ewe may have been infected horizontally during transit or the housing period, a known risk factor for the transmission of SRLV within flocks.[26] This would also suggest that clinical signs developed within 6 months; this relatively rapid progression being more common in cases of visna than with maedi alone.[27] Alternatively, the initial test may have been a false negative or the ewe may have displayed delayed seroconversion.

Although horizontal transmission is an important route of infection both within and between flocks, vertical transmission is known to occur within infected flocks.[21] It therefore seems likely that a proportion of the lambs sold were infected and may well go on to introduce the disease into previously uninfected flocks. Of the animals sold from the flock (total quantity unknown), only one was reportedly returned having been identified as seropositive on quarantine testing; however, other infected lambs may have been admitted to flocks if they had not yet seroconverted or quarantine testing yielded false negatives. Given these risks, the owner's decision to sell lambs as breeding stock is ethically questionable and has placed the referring veterinary surgeon in a difficult position; particularly given the owner has sold lambs to another client of the practice. However, the vet is bound by client confidentiality and can do little more than strongly advise the seller about the potential risks of the sale and remind all clients about the need to consider the health status of all bought in animals. This serves as a stark reminder of the need for good farm biosecurity, and the need for veterinarians to actively monitor the SRLV infection status of their clients' flocks.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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